
Dexamethasone Use in Adult Meningococcal Meningitis

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Abstract

The use of dexamethasone in the management of bacterial meningitis in adults remains controversial. This report illustrates the case of a 27-year-old male with severe meningococcal meningitis and meningococcemia who completely recovered after receiving antibiotics and dexamethasone. In adults with suspected bacterial meningitis, especially in high risk cases, the adjunctive use of dexamethasone may be beneficial.

Case Report

The 27-year-old Indonesian fisherman presented with two days of acute mental status change. He was healthy until he developed an upper respiratory infection five days prior to admission. Three days prior to admission, he had a temperature of 104.8F, occipital headache, and vomiting. Two days prior to admission, he became confused and was unable to recall his own name. His mental status worsened and he had urinary incontinence, and was brought to The Queen's Medical Center.

On exam, his temperature was 101.7F, blood pressure was 98/74, pulse rate was 89/minute, respiratory rate was 16/minute, and oxygen saturation was 98% on room air. He was obtunded. He opened his eyes spontaneously, did not respond to verbal commands, and was able to localize pain stimulus. Neck exam showed marked nuchal rigidity. Muscle tone was normal. Reflexes were diminished. Skin had diffuse petechiae on the trunk, extremities, palms, and soles.

Initial studies showed a hemoglobin of 16.4g/dL and hematocrit of 52.8%, leukocyte count of 9,300/mm³ with 82% segmented neutrophils, normal bands, 10% lymphocytes, and 7% monocytes, and a platelet count of 58,000/mm³. Computed tomography scan of the brain without contrast was normal. Lumbar puncture showed an opening pressure of 33cmH₂O. Cerebrospinal fluid (CSF) was grossly hazy and xanthochromic. CSF leukocyte count was 12,300/mm³ with 94% segmented neutrophils and 6% lymphocytes. No red cells or glucose were detected. Protein was 333mg%. CSF Gram's stain showed 1+ gram-negative diplococci. CSF and blood cultures grew *Neisseria meningitidis*, group C.

In the emergency department, the patient's mental status continued to deteriorate. He was given ceftriaxone 2gm IV empirically. He was admitted to the intensive care unit where he was intubated. Within six hours after receiving of the first dose of ceftriaxone, he was started on dexamethasone 10mg IV q6h for five days. The ceftriaxone was replaced by penicillin G 3.5 million units q4h based on culture and sensitivities for a total antibiotic regimen of ten days.

The patient's fever resolved on hospital day one. On hospital day four, he was able to open his eyes and follow commands. He was extubated and was transferred to the medical floor the next day. He continued to improve, platelet count normalized, and he was discharged from the hospital within three weeks with no sequelae.

Discussion

This case may illustrate the successful adjunctive use of dexamethasone in an adult with severe meningococcal meningitis. On admission, the patient was managed for presumed bacterial meningitis. His prognosis was deemed to be poor based on his deteriorating mental status. Risk factors for death among those with a single episode of community-acquired meningitis include age ≥ 60 years, obtundation on admission, and seizures within the first 24 hours.⁴ The patient's initial studies suggested bacterial meningitis, and he was started on antibiotics and dexamethasone.

During the last 15 years, despite advances in the management of bacterial meningitis, including the introduction of third-generation cephalosporins, there have been no significant reductions in the overall mortality or in the incidence of long-term neurological sequelae following bacterial meningitis.⁷ Bacterial meningitis continues to be associated with high morbidity and mortality. In North America, the case fatality rate for bacterial meningitis by pathogen is: *Streptococcus pneumoniae* 19-46%, *N. meningitidis* 3-17%, *Haemophilus influenzae* 3-11%, and *Listeria monocytogenes* 15-40%.¹

Because evidence from in-vitro studies, experimental animal models, and clinical studies suggest that the host inflammatory response is responsible for much of the serious sequelae of this disease, there is interest in the adjunctive use of antiinflammatory agents in the management of bacterial meningitis. The role for corticosteroids in treating bacterial meningitis may include inhibiting the expression of mRNA for tumor necrosis factor (TNF) and interleukin-1 (IL-1), the production of phospholipid derivatives such as prostaglandins and platelet activating factor, the complement activation, and the activity of the inducible nitric oxide synthetase.⁷ Although clinical trials support the use of corticosteroids in children with bacterial meningitis, especially in those with *H.*

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influenzae type b,^{1,3} there are few data supporting its use in adults.

In 1988, Label *et al* first reported that the use of dexamethasone was associated with protection against hearing loss in childhood *H. influenzae* type b meningitis. It was recommended for routine use in childhood *H. meningitis* in 1994.⁵

Since 1988, there has been only one trial involving the adjunctive use of dexamethasone in adults with bacterial meningitis. In a prospective, randomized trial involving 147 adults (≥ 13 -years old) and 282 children with bacterial meningitis, Girgis *et al* found significant reduction in the case fatality rate and neurological sequelae in patients receiving dexamethasone. The breakdown of the 429 cases were: *N. meningitidis* 267, *S. pneumoniae* 106, and *H. influenzae* 56. Dexamethasone was given at 8 mg IM q12h to patients <12 -years old and at 12 mg IM q12h to patients ≥ 12 -years old for three days, starting with first dose of antibiotics. They found a reduction in case fatality rate. Twenty (5 adults and 15 children) of 210 patients died among those who received dexamethasone, compared with 42 (18 adults and 24 children)/219 died among those who did not receive dexamethasone ($p < 0.01$). The reduction in case fatality rate was statistically significant only in patients with *S. pneumoniae* meningitis, in which 7/52 patients receiving dexamethasone died compared with 22/54 patients not receiving dexamethasone died ($p < 0.002$). They also found a reduction in neurologic sequelae, *ie.* hearing impairment and paresis, in patients receiving dexamethasone. This was also statistically significant only in patients with *S. pneumoniae* meningitis, in which 0/45 surviving patients receiving dexamethasone had severe hearing loss, compared with 4/32 patients not receiving dexamethasone had severe hearing loss ($p < 0.05$). They found no significant difference between those who did and did not receive dexamethasone for the time it took them to become afebrile or to regain consciousness, or in the mean admission and 24- to 36-hour CSF leukocyte count, glucose or protein content.⁶

In a review of treatment of bacterial meningitis, Quagliarello and Scheld recommended adjunctive dexamethasone therapy in children >2 -months old who have bacterial meningitis, particularly those thought to be infected with *H. influenzae*, *ie.* in children not vaccinated against *H. influenzae* and those with CSF showing gram-negative coccobacilli. They believed in a more limited use of dexamethasone in adults with bacterial meningitis, especially to those with a high concentration of bacteria in CSF, *ie.* those with positive CSF Gram's stain, and evidence of increased intracranial pressure. For those children and adults, they recommended starting dexamethasone at 0.15 mg/kg body weight IV q6h for four days with or slightly before the first dose of antibiotics.²

While corticosteroids could theoretically reduce the penetration of antibiotics into the central nervous system, there is no clinical evidence to support this.⁷ In a meta-analysis of randomized clinical trials since 1988 involving dexamethasone as an adjunctive therapy in bacterial meningitis involving primarily children, McIntyre *et al* found that adverse effects from dexamethasone use was only significant for secondary fever, but not for delayed CSF sterilization, late seizures, reactive arthritis, mortality or gastrointestinal tract bleeding.⁵ Furthermore, the empirical use of dexamethasone with antibiotics for suspected bacterial meningitis in patients with aseptic meningitis appears to be safe. In a retrospective analysis of 32 children with suspected bacterial meningitis, there were no adverse

effects associated with the use of dexamethasone even in those with nonbacterial infections or positive viral cultures.⁷

Regarding the timing and duration of dexamethasone regimens, Townsend and Scheld suggested starting it before or at the same time as the start of antibiotics, since the synthesis of TNF and IL-1 occur after the antibiotic-induced lysis of bacteria and exposure of cell surface components.⁷ A meta-analysis of randomized clinical trials by McIntyre *et al* found that a two-day and four-day dexamethasone regimen resulted in similar outcomes, and is associated with a lower risk of gastrointestinal tract bleeding, and that a one-day regimen may be ineffective.⁵

Conclusion

There are no uniform guidelines for the adjunctive use of dexamethasone in adult bacterial meningitis. Because of the benefits demonstrated in childhood cases, and the potential benefits of antiinflammatory agents, one may consider using dexamethasone in adults with suspected bacterial meningitis, especially in high risk cases. In this case, dexamethasone 10 mg IV q6h for five days was started within six hours of initiating the antibiotic regimen in a patient with presumed bacterial meningitis and deteriorating mental status, and he recovered without sequelae.

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